UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/808,522	03/25/2004	Wei Liu	01997.001800	6560

45743 7590 07/28/2006

FITZPATRICK CELLA (WYETH)
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112-3800

EXAMINER	
SWOPE, SHERIDAN	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 07/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/808,522	LIU ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *1-18 and 20-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *25 March 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1104; 0205*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election, without traverse, of Invention II and sub-invention (A), Claims 19 and 47, in their response of June 13, 2006 is acknowledged. Claims 1-47 are pending. Claims 1-18 and 20-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 19 and 47 are hereby examined.

Priority

The priority date for the invention of Claim 19 is taken to be March 25, 2003, the filing date of US 60/456,958, which discloses SEQ ID NO: 1 & 2, while the priority date for the invention of Claim 47 is taken to be March 25, 2005, the filing date of the instant application, which discloses the genus of polypeptides having at least 97.2% homology to SEQ ID NO: 2.

Drawings-Objections

Figures 6 and 7 are objected to for disclosing sequences, that are not identified by a sequence identifier number (SEQ ID NO:). The sequence rules embrace all nucleotide sequences with ten or more bases and all amino acid sequences with four or more amino acids. Said sequences must be disclosed in a sequence listing and identified by a specific SEQ ID NO: (MPEP 2421.02). 37 CFR 1.821(d) requires the use of the assigned sequence identifier number in all instances where the description or claims of a patent application discuss sequences, regardless of whether a given sequence is also embedded in the text of the description or claims of an application. Applicant is required to correct the figures, or legends thereto, to identify all of the sequences disclosed therein by sequence identifier numbers.

Specification-Objections

The specification is objected to for containing hyperlinks, for example on page 34. USPTO policy does not permit the USPTO, i.e, via an issued patent, to link to any commercial sites, since the USPTO exercises no control over the organization, views or accuracy of the information contained on these outside sites. Hyperlinks and other forms of browser-executable code, especially commercial site URLs, are not to be included in a patent application. (MPEP 608.01) The specification should be completely and carefully checked and all URLs removed.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Utility

Based on the title and the specification, page 1, paragraph 2, the asserted utility for the protein of SEQ ID NO: 2 is as a protein kinase. Said asserted utility is not specific, substantial, and credible for the following reasons. First, the specification fails to provide experimental evidence that the protein of SEQ ID NO: 2 has protein kinase activity. Second, neither the specification nor the prior art providence evidence that the protein of SEQ ID NO: 2 is homologous to any polypeptide with demonstrated protein kinase activity. Third, even if the skilled artisan believed that, more likely than not, the polypeptide of SEQ ID NO: 2 is a protein kinase, said assertion is not specific and substantial. The family of protein kinases is a large and variable family of enzymes with the with a large number of variable substrates; specific substrates for the polypeptide of SEQ ID NO: 2 have not been identified.

Nonetheless the specification provides a specific, substantial, and credible utility for the protein of SEQ ID NO: 2. At page 44, line 6, Applicants asserts that the polypeptide of SEQ ID

NO: 2 suppresses programmed cell death. In support of said assertion, Example 4 discloses that heterologous expression of the protein of SEQ ID NO: 2 protects against staurosporine- and etoposide-induced apoptosis (pg 44-45). The protein of SEQ ID NO: 2 is as effective as the Bcl-x_L polypeptide, a known anti-apoptotic protein. Thus, Applicants' assertion that the polypeptide of SEQ ID NO: 2 suppresses programmed cell death is specific, substantial, and credible. Moreover, the protein of SEQ ID NO: 2, and the encoding polynucleotide, have real-world use in the molecular and cellular investigation of apoptosis.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "having" renders Claim 19 indefinite because it is unclear whether said term means "comprising" or "consisting of". Clarification is required. For purposes of examination, it is assumed that "having" means "consisting of".

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 19 and 47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 2, does not reasonably

provide enablement for any peptide fragment of SEQ ID NO: 2 or any polypeptide having at least 97.2% homology to SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In regards to this enablement rejection, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claim 19 is so broad as to encompass any polypeptide fragment of SEQ ID NO: 2, wherein the fragment has any activity. Claim 47 is so broad as to encompass any polypeptide having at least 97.2% homology with SEQ ID NO: 2, wherein the polypeptide has any or no activity. The scope of these claims is not commensurate with the enablement provided by the disclosure with regard to the large number of polypeptides encompassed. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's

sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the polypeptide of SEQ ID NO: 2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications for any desired activity, as encompassed by the instant claims. Furthermore, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable (Galye et al, 1993; Whisstock et al, 2003). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of Claim 19 which, encompasses all peptides fragments of SEQ ID NO: 2 having any activity. The specification does not support the broad scope of Claim 47 which, encompasses all polypeptides having at least 97.2% homology with SEQ ID NO: 2 having any or no activity. The specification does not support the broad scope of Claims 19 and 47 because the specification does not establish: (A) the desired activity for fragments of SEQ ID NO: 2; (B) which fragments of SEQ ID NO: 2 have the desired activity; (C) a rational and predictable scheme for choosing the fragments of SEQ ID NO: 2 having the desired activity; (D) how to use any polypeptide having at least 97.2% homology to SEQ ID NO: 2; (E) the desired activity for any polypeptide having at least 97.2% homology with SEQ ID NO: 2; (F) regions of SEQ ID NO: 2 that can and cannot be altered and retain the desired activity; (G) a rational and predictable scheme modifying the polypeptide of SEQ ID NO: 2 to obtain

polypeptides having at least 97.2% homology with SEQ ID NO: 2 and having the desired activity; (H) the specification provides insufficient guidance as to which of the essentially infinite possible choices of fragments and variants of SEQ ID NO: 2 are likely to have the desired activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of fragments and variants of SEQ ID NO: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of the FXR-mediated actions and methods of repressing said actions having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claims 19 and 47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of protein molecules that are either a fragment of SEQ ID NO: 2 or have at least 97.2% homology with SEQ ID NO: 2.

The specification does not contain any disclosure of the function of said protein molecules. The genus of peptides and polypeptides that comprise these above protein molecules is a large variable genus with the potentiality of having many different activities. Therefore,

many functionally unrelated protein molecules are encompassed within the scope of these claims. The specification discloses the function of only a single species of the claimed genus, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Sigma, Inc., 1997 or Plowman et al, 2001. Sigma, Inc teach a fragment consisting of residues Glu^{376}-Gly^{377} of SEQ ID NO: 2, while Plowman et al teach a fragment consisting of residues 6-360 of SEQ ID NO: 2. Therefore, Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Sigma, Inc., 1997 or Plowman et al, 2001.

Claim 19 is rejected under 35 U.S.C. 102(a) as being anticipated by Strausberg et al, 2002. Strausberg et al teach the polypeptide of SEQ ID NO: 2. Therefore, Claim 19 is rejected under 35 U.S.C. 102(a) as being anticipated by Strausberg et al, 2002.

Claim 47 is rejected under 35 U.S.C. 102(b) as being anticipated by Strausberg et al, 2002. Strausberg et al teach the polypeptide of SEQ ID NO: 2. Therefore, Claim 47 is rejected under 35 U.S.C. 102(b) as being anticipated by Strausberg et al, 2002.

Claims 19 and 47 are rejected under 35 U.S.C. 102(e) as being anticipated by Whyte et al, 2004 (priority date July 17, 2002). Whyte et al teach the polypeptide of SEQ ID NO: 2. Therefore, Claims 19 and 47 are rejected under 35 U.S.C. 102(e) as being anticipated by Whyte et al, 2004.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheridan Lee Swope, Ph.D.
Art Unit 1656